ENCLOSURE B

Revised Charge and Discussant Assignments

General Purpose: Review the Mode of Action Determination and Selection of Nonlinear Dose-Response Approach for Chloroform under EPA's Proposed Cancer Risk Assessment Guidelines Revisions, and advise on any needed revisions to the Cancer Guidelines as indicated by their application in this instance.

Charge 1: Based on its application to the chloroform risk assessment, please identify any specific text in the draft Cancer Risk Assessment Guideline's framework for mode of action analysis (section 2.5) which you would advise be changed prior to their publication. **ASSIGNMENTS:** ***All Subcommittee Members (see discussion in letter)***

Charge 2: **Specific questions:**

a) In the draft chloroform risk assessment document, are the conclusions as to the following issues adequately supported by the analyses presented in the health risk assessment/characterization (as supported by the ILSI report) and the framework analysis?

i) chloroform's mode of action **ASSIGNMENTS**: ***Dr. Maronpot Lead; Dr. Klaunig, Associate***

ii) consideration of a nonlinear approach to dose-response, and the possibility that mutagenesis might play a role in the carcinogenic response. **ASSIGNMENTS:** ***Dr. Zeise Lead; Dr. Ray, Associate***

iii) the relationship of low-dose pathology to the doses that induce tumors. **ASSIGNMENTS**: ***Dr. Klaunig, Lead; Dr. Maronpot, Associate***

iv) epidemiologic evidence on chlorinated drinking water as to the carcinogenicity of chloroform, including comment on any conclusion to be drawn from the epidemiologic data about mode of action. **ASSIGNMENTS**: ***Dr. Savitz, Lead; Drs. Zeise and Bull, Associates***

b) Does the assessment of children's risk for chloroform appropriately address the risk concerns including ontogeny of drug metabolizing enzymes), given the data available? **ASSIGNMENTS:** ***Dr. Lambert, Lead; Drs. Davis and Okita, Associates***